Author's response to reviews

Title: The impact of social deprivation on mortality following acute myocardial infarction, stroke or subarachnoid haemorrhage: A record linkage study

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Author's response to reviews: see over
Dear Editor,

Thank you for considering our research for publication in your journal. We are grateful for the reviewers’ comments and have addressed each of them as described below.

**Reviewer 1 comments**

1) Overall, a more in depth background section providing additional context for the reader would improve the manuscript. It would be helpful to introduce issues such as greater specificity of the severity and scope of the problem (e.g. high mortality) and what mechanisms are proposed to explain the hypothesized deprivation inequalities in mortality for the 3 conditions.

We have added additional text to the Introduction (lines 54 to 56 and 61 to 69) to provide additional background information on social deprivation and mortality risk in acute myocardial infarction, stroke and subarachnoid haemorrhage.

2) Reading the background I am also unclear what the proposed study will add to the debate of social deprivation and mortality following acute myocardial infarction, stroke or subarachnoid haemorrhage. A few sentences discussing a specific contribution would strengthen the paper.

We have added additional text to the Introduction highlighting the lack of published literature on the subject, particularly for risk factors (lines 61 to 65) to provide a strong rationale for the need for this research.

3) A significant limitation to the paper was the second objective of “determine how any increased mortality for deprived groups may be affected by factors such as patient demographics, timing of admission and hospital size”. Including a greater discussion and rationale in the background for the second objective would support investigation of the proposed associations.

We have added additional text to the Introduction (lines 61 to 69). As no literature exists on the impact of other key factors such as day of the week, year of admission and hospital size, we have hypothesised why any differences might occur.

4) Continuing on with the second objective, in the “methods” section under “risk factors”, it is not clear how patient demographics, timing of admission and hospital size are hypothesized to influence the association between social deprivation and mortality. For example, are they considered confounders of the relationship or mediators?

We would hypothesise that most of the risk factors being analysed are mediators of the relationship. The text in the Introduction now outlines this (lines 61 to 69).

5) In the “Risk factors” section it was described that to assess the impact of risk factors on the relationship between social deprivation and mortality (i.e. to compare the least and most deprived cases using the least deprived quintile as the reference group). As written, I am not clear what methodology has been used. In particular when in the “Methods and analysis” section, paragraph 2 it describes that logistic regression was used to assess whether “increased mortality for deprived groups may be affected by key risk factors including patient demographics...” I am not clear how this produced the results presented in Table 2.

We have written a more detailed description of the methodology and described how we used each subgroup within each risk factor and used logistic regression to compare the mortality risk of the most deprived group with the least deprived group (as a comparison) (lines 133-135).

6) In the “Results” section, “effect of factors on the increased mortality with social deprivation” section, – The results presented in this section and in Table 2 are not clear. As mentioned in the methods section, it remains unclear what regressions are determining the presented odds ratios. Are these the odds of mortality given social deprivation stratified by each level of the risk factors?


Having clarified the methodology used in this paper, we think that the existing text in this section is now appropriate. If the Editor feels that we need to clarify our results we would be happy to oblige.

7) In the discussion section, paragraph 1, s-to sentence 2: Based on the analysis, I am not able to evaluate this sentence based on the evidence provided.

We have reworded the paragraph to clarify our summary of the findings (lines 267-70).

8) In the “patient comorbidities” section, it is unclear how the factors discuss play into the analysis in this study. Specifically, they are not mentioned again throughout the manuscript, with the exception of appearing as a limitation in the “discussion” section, final paragraph. This is extremely important potential source of confounding that should be quantified in this study. Further the sentence “This methodology is described elsewhere [27]” is not appropriate. Please describe any methodology used to adjust for patient comorbidities in this study. Were any other confounders considered besides age and sex?

We have elaborated on the methodology used to measure and adjust for patient comorbidities in the methods section (lines 156 to 162). Only age, gender and comorbidities were included as potential confounders to adjust for. We have used this methodology in other publications.


We have also removed the “This methodology is described elsewhere [27]” sentence but retained the reference as we feel that it is relevant to indicate that this methodology has been used in other published work.

9) In the “Methods of analysis” section, paragraph 2 the analytical approach described uses logistic regression to achieve the study outcomes. Please describe the rational for not using a time to event analysis (e.g. cox proportional hazard model). It is assumed that the time to event is available given that mortality at different time points is being assessed.

We opted to use logistic regression as our main study outcome measure was short-term mortality at 30 days. Logistic regression is used much more extensively for short term mortality than time to event analysis (Cox’s model). The authors have used Cox’s model for longer term follow up on other studies.


10) In the “Methods” section, “study design”: a few details could be added if appropriate for this data linkage study. Mainly: 1) what percentage of patients were able to be linked to other data sources (e.g. to the SAIL, ONS and AR)?; 2) what percentage of all deaths to study subjects were ascertained in the ONS and AR? 3) Was there any other missing data? For example, in the footnotes to Table 1 you have specified “Gender for 1 case was not recorded for AMI, WIMD score was available for 3.2% of AMI cases”.

All patients included in our study had an Anonymised Linking field (ALF) ID assigned to them, allowing them to be accurately linked to national databases such as the Office of National Statistics and the Welsh Administrative Register. As such, there is 100% coverage of potential mortality for all cases. We have elaborated on this in the article (line 94) and added two references explaining the linking process.


Ford DV, et al., The SAIL Databank: building a national architecture for e-health research and
Missing variables are already described in Tables 1 and 2 as footnotes. We have now included a section in the “Methods of analysis” section (lines 189 to 192).

11) In the “Methods” section, under “Study design”, second paragraph: This section could be written with more detail to facilitate clarity for readers not familiar with the datasets used in the study.

We have expanded the sections on linking with mortality and primary care datasets and included a key reference regarding the data and methodology.

12) In the “Inclusion and exclusion criteria” section: it is stated that all emergency admissions to Welsh hospitals were selected for AMI, stroke or SAH. What is the coverage for your study for events (e.g. AMI mortality) that were not admitted to an emergency hospital (e.g. those that died in the community)? If a large amount this should be discussed in the limitations section.

Our study investigated post-hospital mortality for AMI, stroke and SAH, so did not include deaths that occurred rapidly before admission to hospital. We have explained this on lines 279 to 280.

13) In the “Mortality” section, can you provide a rational for choosing to look at 30 day mortality? Also, in the first sentence 365 days was mentioned as a secondary outcome but no results were discussed in the manuscript.

We chose 30 day mortality as a primary outcome measure after taking clinical advice and also since it is the most widely used measure in the literature. We reported mortality rates at 365 days in the “mortality and social deprivation” section of the results but have now also included it in Table 1.

14) In the “Social deprivation” section, it is not clear whether the domains of deprivation are based on individual characteristics, or whether they relate to community/neighbourhood level percentages.

We have further clarified in the text that it is an area-based measure (lines 125 to 126).

15) In the “Methods of analysis” section, the first sentence reads “the main study outcome measures were percentage mortality rates at 30 days...”. Is the main study outcome not the increased odds of mortality in low compared to high deprivation as would be suggested by the use of logistic regression analyses?

We have rewritten the text to clarify that the main outcomes were mortality rates and odds of mortality for quintile V versus I, with seven and 365d mortality rates and odds of mortality as a secondary outcome measures (lines 170 to 172).

16) In the “Methods of analysis” section, paragraph 2, sentence 1: “any increased risk”, should read “any increased odds” given that a logistic regression has been used.

We have amended the text to replace and occurrences of “risk” with “odds” where appropriate (line 174).

17) In the “Methods of analysis” section, paragraph 2, sentence 4: I don’t see Bonferroni correction as necessary given the statistical test described in this manuscript. Was there multiple statistical tests performed that were not outlined in the method section? If so, please provide a description of statistical testing undertaken.

We opted to add Bonferroni testing for the multiple factors and tests presented in Tables 1 and 2 in light of past reviewer comments on similar papers. We feel that this strengthens the paper and would prefer to retain the additional test for added rigour.

18) In the “Results” section, it would be helpful to have Table 1 describe admissions and mortality rates by social deprivation for each of the risk factors and patient comorbidities. Could move any odds ratios to a second table.
We are not sure what the reviewer is suggesting as it appears to be overly complicated to present. If we could receive clarification, we would be happy to oblige.

19) In the “Results” section– The results from logistic regression analyses are not interpreted correctly. It is an increase odds, not a percentage. This continuous throughout the whole section. Ideally the odds ratio and 95% confidence intervals would be presented for each association discussed.

We have chosen to report our regression results in the text using percentages equivalent to the odds ratios, which are already listed in the relevant tables, to help readers understand the results. We have done this in other published research with no objections. If the editor wishes us to amend the text to report the odds ratios instead of their % equivalents, we would be happy to oblige.

20) In the “Results” section– At some point in the manuscript it would be appropriate to perform a power analysis to determine whether there is enough sample size to find an association between social deprivation and mortality for the SAH outcome.

We have added text describing the sample sizes needed to detect increased mortality for the most deprived quintile compared with the least deprived.

21) In the discussion section, paragraph 6, sentence 4: A clear rationale for why seasonal variations in the social inequalities in mortality would be expected. If, as suggested, that an increased population-based mortality during summer months was related to air pollution, would this not effect more and less deprived areas equally? Are there other potential mechanisms?

Having tested for any interaction effect between social deprivation and season (suggested by reviewer 2) and found none, we have opted to remove the text.

22) In the discussion section, paragraph 7, sentence 1: Results from a time trend analyses were not presented in the study. Please include this analysis in the manuscript if this is of interest to the authors.

We have edited the text as we were not describing a time trend analysis. We have clarified that we were analysing the differences between different year groupings and discussed those findings (lines 298 to 301).

Reviewer 2 comments

23) For the results presented in table 2, the authors focus on interpreting whether odds ratios of high deprivation versus low deprivation differ between strata. This is fine to present, but it seems that the question they propose is not whether these differ from the null, but whether the estimates in strata differ from each other. That is, effect modification. The authors should clarify their intent here, but from my perspective at least testing for interaction would be more useful to present and interpret. For example, in a number of cases (e.g. hospital size for stroke) odds ratios are very similar, it just happens that for one of them the results are not quite statistically significant. This does not mean that the associations with social deprivation differ in these contexts.

We have tested for interactions between social deprivation and each risk factor and added the methodology (lines 180 to 181) and results to the paper (lines 253 to 256).

24) Why are the one year follow-up rates described in the methods not shown in Table 1 or Table 2? Also, in Table 2 the title indicates that mortality at 7 days should be shown but this is not shown in the table.

We have added the 365 day mortality data to Table 1. Table 2 focusses solely on our primary outcome measure of mortality at 30 days and as such, seven and 365 day mortality were not included. We have removed the error in Table 2’s title stating incorrectly that it reported on 7 day mortality.

25) In a few places the authors write “affected” but throughout it would be more accurate to say correlated
We have amended our text to replace “affected” with “correlated” where appropriate.

26) It would be useful to have a discussion of what “hospital size” is suggested to be capturing. Is this being used to proxy quality of care?

We selected hospital size as a proxy for resource availability which can be considered one possible measure of quality of care. We hypothesised that larger hospitals might have increased capacity and more, albeit specialist, facilities, equipment and staff compared with smaller hospitals.

27) It would be more accurate to write “higher” rather than “increase” when describing the results since the analysis is not actually looking at change in social deprivation as the exposure. Similarly when the term “decrease” was used.

We have amended our text to replace “increased” with “higher” and “decreased” with “lower” where appropriate.

28) In limitations, I think that it would be more accurate to say that area social deprivation is a mixed exposure that due to economic segregation is correlated with both individual and area characteristics.

We appreciate the reviewer’s advice and have added his suggested text to our discussion (lines 320 to 321).

29) The discussion paragraph that begins “Our study found no trend over time…” should be clarified. Does this mean no differential grand over time? The following sentences in this paragraph don’t seem to fit with the first paragraph. Either way, what is meant here should be clarified.

See the response to a comparable comment by reviewer 1 (comment 22).